This study investigated data of 1,063 adolescents aged 12-18 years from the fifth and sixth Korea National Health and Nutritional Examination Survey (2009-2011). The association of various factors (vitamin D level, calcium intake, body mass index (BMI), lean mass, fat mass, and physical activity) with BMD Z-scores in whole body, lumbar spine, total femur, and femur neck were analyzed. We defined vitamin D deficiency (≤ 12 ng/mL), vitamin D insufficiency (12-20 ng/mL), and sufficiency (> 20ng/mL) according to the 25-hydroxyvitamin D (25-OHD) level. We analyzed association between BMD and vitamin D levels after adjusting for other factors.
Results
The mean 25-OHD level of subjects was low (16.28 ng/ml). Of all subjects, 21.9% were vitamin D deficient, and 58.5% were vitamin D insufficient. Among the vitamin D groups, the vitamin D sufficient group had significantly higher BMD Z-scores than the vitamin D deficient group in whole body, lumbar spine, and femur neck. The sufficient vitamin D group had higher BMD Z-score than the vitamin D insufficient group in femur neck, and the vitamin D insufficient group had higher BMD Z-score than the vitamin D deficient group in whole body. Among various factors, vitamin D status, calcium intake, BMI, lean mass, fat mass, and physical activity were positively associated with BMD Z-scores. In particular, lean mass was the strongest independent factor. Vitamin D levels were positively associated with the BMD Z-scores even after adjusting for other factors.
Conclusions
Vitamin D deficiency and insufficiency were common among adolescents. This study suggested that vitamin D level was positively associated with BMD, and that sufficient vitamin D level was needed to prevent low BMD. Vitamin D status is an important factor of BMD in adolescents.

Thyroid

HPT-AXIS AND THYROID HORMONE ACTION

Phenotype and Genotype Analysis of Patients with Resistance to Thyroid Hormone β: A Single-Center Experience

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Introduction Resistance to thyroid hormone β (RTHβ) is caused by mutations in *THRB*, the gene that encodes thyroid hormone receptor β. The clinical phenotype is variable and may include goiter, tachycardia, and learning disability with or without hyperactive behavior. The biochemical hallmark of RTHβ is elevated T4 and T3 with non-suppressed TSH concentrations. We here describe the phenotype and genotype of three Thai patients diagnosed with RTHβ in a pediatric referral center. Patients had previously been misdiagnosed and inappropriately treated with antithyroid drugs (ATDs). **Methods** Clinical features and thyroid function tests (TFTs) of three unrelated RTHβ patients were retrospectively reviewed. Genomic DNA of the RTHβ patients and affected family members was amplified for exon 7-10 of the *THRB* gene and sequenced to identify mutation by Sanger sequencing. The impact of the p.L341V novel mutation on the affinity for T3 and T3-induced transcriptional activity was previously determined *in vitro*. **Results** Three female patients were diagnosed with RTHβ. All of them had been misdiagnosed with hyperthyroidism and treated with ATDs prior to referral. The mean age at diagnosis was 8 years. The main presenting symptoms were diffuse goiter and tachycardia. The mean duration of ATD treatment was 3 years. During the treatment, patients had fluctuating thyroid hormone and increased TSH levels. An older sister and mother of one patient also had similar TFTs abnormalities, for which the mother had undergone a subtotal thyroidectomy. RTHβ was diagnosed based on the high FT3 and FT4 with normal (non-suppressed) TSH concentrations and confirmed by mutation analysis. Anti-thyroid peroxidase, anti-thyroglobulin, and TSH receptor antibody (TRAb) were negative, excluding autoimmune thyroid disease. Heterozygous missense mutations of the *THRB* gene were identified in all patients and affected family members. Two mutations had been previously reported (p.R243W and p.L456F), and one mutation was novel (p.L341V). *In vitro* studies confirmed an important role of Leu341 in T3 binding of the TRβ and functional impairment of the p.L341V novel mutation and were reported separately. According to available literature, only nine Thai RTHβ patients (in three families) carrying three different mutations (p.G251V, p.M313T, and p.A317T) had been previously reported. Goiter was the most common clinical finding, and almost all patients had a history of receiving unnecessary treatment with ATDs. **Conclusion** We report a series of RTHβ patients carrying *THRB* gene mutations, including one novel mutation (p.L341V). Clinicians should be alert that RTHβ can be found in patients with goiter and tachycardia. Elevated T4 and T3 with non-suppressed TSH concentration is the main diagnostic clue for this disease. Mutation analysis allows definitive diagnosis of RTHβ and may help to avoid potential misdiagnosis and improper treatment.

Reproductive Endocrinology

MALE REPRODUCTIVE CASE REPORTS

Digenic Inheritance of PCSK1 and CHD7 Mutations in PAX4 Homozygous Diabetic Male with Normosmic Hypogonadotropic Hypogonadism

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Background: Normosmic congenital hypogonadotropic hypogonadism denotes Kallmann syndrome not associated with anosmia or hyposmia. Over the past few years, the availability of next-generation sequencing has started to unravel the complex molecular basis of congenital hypogonadotrophic hypogonadism including digenic or oligogenic pathogenecity in addition to classic monogenic causality (1).